

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



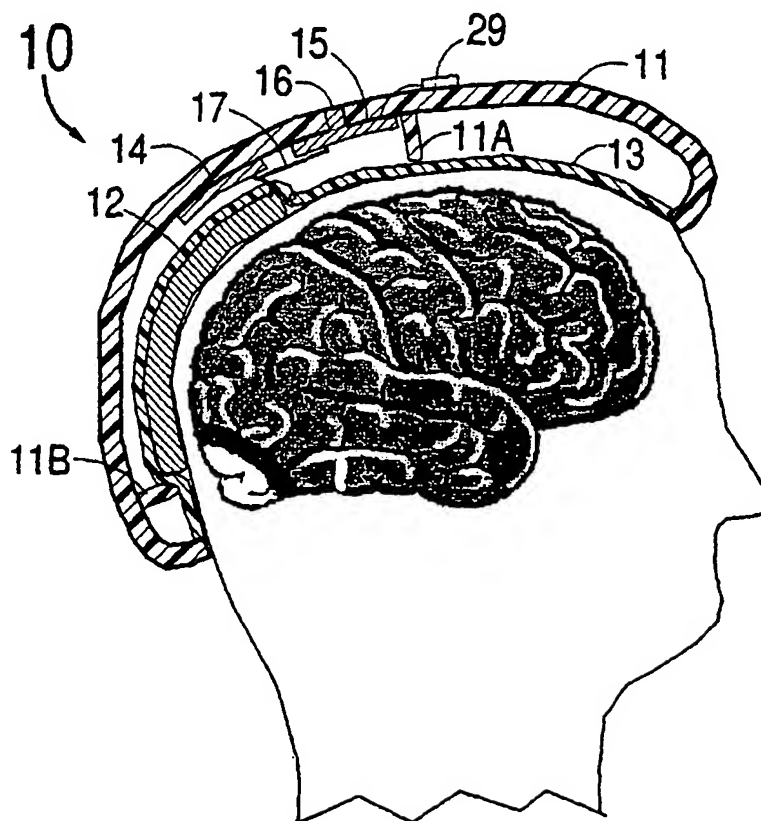
(43) International Publication Date
7 February 2002 (07.02.2002)

PCT

(10) International Publication Number
WO 02/09811 A1

- (51) International Patent Classification⁷: A61N 2/02 Adrian, R., M.; 78 Highland Park Drive, Dundas, Ontario L9H 6G8 (CA).
- (21) International Application Number: PCT/US01/23958
- (22) International Filing Date: 31 July 2001 (31.07.2001) (74) Agent: WIXON, Clarke; NeuroPace, Inc., 255 Santa Ana Court, Sunnyvale, CA 94085 (US).
- (25) Filing Language: English (81) Designated States (*national*): CA, JP.
- (26) Publication Language: English (84) Designated States (*regional*): European patent (DE, FR, GB).
- (30) Priority Data:
09/629,210 31 July 2000 (31.07.2000) US Published:
— with international search report
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
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- (72) Inventors: FISCHHELL, Robert, E.; 14600 Viburnum Drive, Dayton, MD 21036 (US). FISCHHELL, David, R.; 71 Riverlawn Drive, Fair Haven, NJ 07704 (US). UPTON, For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: MIGRAINE HEADACHE TREATMENT APPARATUS



(57) Abstract: A system and method for treating migraine headaches employs a readily portable and easy-to-operate head-mounted magnetic depolarizer (10) to generate a transient or alternating high-intensity magnetic field in and around the user's occipital lobe or other portion of the brain (1), thereby terminating the spreading depression phenomenon characterizing a migraine headache and its aura.

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MIGRAINE HEADACHE TREATMENT APPARATUS

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FIELD OF THE INVENTION

10 This invention is in the field of medical devices for the treatment of migraine headaches.

BACKGROUND OF THE INVENTION

15 Migraine headaches occur in approximately 12% of the world population. Therefore, in the United States in the year 2000 there are approximately 30 million people who suffer from this affliction. Although medicines have been created that significantly diminish the suffering of migraine patients, the medicines often have highly undesirable side effects and many patients do not obtain satisfactory relief from the severe headache pain and other
20 discomforts associated with migraine. Furthermore, migraine headaches are typically treated after they have become painful, i.e., the treatment is often ineffective in preventing the onset of the migraine headache. Other than some drugs for some patients, there is no known treatment for migraine headaches that can be applied after a patient detects an aura of that headache to prevent the occurrence of pain and other undesirable manifestations of that
25 migraine headache. A non-invasive, non-drug method for preventing the occurrence of migraine headaches would be a remarkable boon for those millions of people all over the world who suffer from these painful experiences.

 In 1985, A.T. Barker, et al (Lancet, 1985, pp. 1105-1107) described the use of a coil placed over the scalp which produced a high intensity, time varying, magnetic field. This
30 magnetic field produces an electric current in the cortex of the human brain which can in turn produce certain effects on brain neurons. By the year 2000, this type of system was given the name Transcranial Magnetic Stimulation (TMS). If repetitive magnetic pulses are applied in this manner, it has been given the name rTMS.

In the journal Neurology (April 11, 2000, pp. 1529-1531), it has been reported by B. Boroojerdi, et al that rTMS at a rate of one pulse per second can create a reduction of the excitability of the neurons of the human visual cortex. However, no known references have indicated that rTMS can be used for the preventing the occurrence of migraine headaches.

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SUMMARY OF THE INVENTION

This invention is a means and method for the treatment of migraine headaches for those patients who experience a distinct aura before the actual occurrence of the symptoms of the migraine headache. It is estimated that approximately 40% of all migraine patients have a distinct aura that is a precursor of a migraine headache. Approximately half of these patients have a visual aura that typically begins as a small pattern of scintillating colored lights that have the appearance of wiggling worms. Over a time period of between 20 and 30 minutes, the pattern enlarges until it occupies nearly the entire visual field. During this time period, the patient might also completely lose part of his visual field. At the end of this visual aura, most migraine patients have a severe headache that is often accompanied by other symptoms such as nausea, vomiting and other unpleasant feelings. Many migraine patients who do not have a visual aura have some other precursor of a migraine that can be perceived from minutes to hours before the actual start of the headache.

The visual aura is a result of the spatial progression of a band of brain cells that are excited in that band across one half of the brain's occipital lobe. This band moves in an anterior direction at the rate of approximately 2-5 mm per minute. It is this excited band of neurons of the brain that produces the scintillating colored lights that are perceived by the patient as an aura that is a precursor of a migraine headache. Behind this leading band of excited neurons, a spreading region of neurons with depressed electrical excitability occurs. This phenomenon is known as "the spreading depression of Leao".

It is believed that if the advancing band of excited neurons can be stopped before the aura has completed its 20 to 30 minute time duration period, the migraine headache will not occur. One way to stop such an advancing band of excited brain neurons would be by imposing a high enough electric current through these neurons so that they become depolarized. This could be accomplished by means of electrodes placed on the brain's surface at the occipital lobe (i.e., the visual cortex). If these electrodes would have at least several milliamps of electrical current placed across them, the excited neurons could be

depolarized, thus eliminating their enhanced excitability. However, this would require surgery to implant such electrodes. Also, a neurostimulator attached by wires to the electrodes would be required, which neurostimulator would be adapted to place a voltage across the electrodes to cause the flow of a sufficiently high electrical current to depolarize the advancing band of excited neurons.

The invention disclosed herein is a non-invasive, externally applied device that is placed on or near the patient's head in the region of the brain where the aura originates (e.g., the occipital lobe) as soon as possible after the patient becomes aware of a visual (or any other type) aura that is a precursor of the migraine headache. For patients whose aura originates from a region of the cerebral cortex that is not the occipital lobe, the depolarizing device can be applied to that region of the brain. By the use of a high intensity alternating magnetic field, a sufficiently high electrical current can be placed onto the advancing band of excited neurons so as to depolarize those neurons thereby terminating the aura before it is able to progress into a migraine headache. Depolarization of neurons in advance of the advancing band of excited neurons may also be used to prevent a migraine headache. This is because depolarized neurons become refractory after rTMS is applied. This is analogous to cutting down or burning the trees in front of a forest fire in order to prevent the spread of that forest fire.

The one pulse per second of rTMS described by Boroojerdi, et al, which was proven to cause a reduction of cerebral cortex excitability, could be applied to break up the advancing band of excited neurons that is the cause of the visible aura of a migraine headache. Since an aura has a time duration that is typically at least 20 minutes, the patient has a sufficient time period for placing the rTMS magnetic depolarizer in the appropriate position for it to be effective in depolarizing the advancing band of excited brain neurons.

It should also be noted that stimulation of the scalp might also have an effect in preventing or decreasing the severity of a migraine headache for at least some patients. Scalp stimulation may act as a conditioning response that becomes associated with the migraine process. Pairing this response with rTMS may provide cessation of the migraine process with progressively less intensity of magnetic stimulation.

Since the band of excited neurons that create a visual aura moves from the back of the head in an anterior direction, and since either the left or right half of the occipital lobe might be involved, the magnetic depolarizer would optimally be placed along the posterior-anterior centerline at the top of the head. If it is known that a particular patient has the spreading

depression on either the right or the left half of the occipital lobe, then the magnetic depolarizer might be placed only on that region where the spreading depression occurs. If the aura originates from a part of the cerebral cortex that is not the occipital lobe, then the alternating magnetic field can be appropriately placed to depolarize neurons in that location.

- 5 It is expected that the patient can be trained to recognize the symptoms from a particular area of the brain so that the magnetic depolarizer can be placed in an optimum location to prevent the occurrence of a migraine headache.

The magnetic depolarizer can be formed in a race-track, figure-eight shape with its long axis placed along the head's posterior-anterior centerline. The width of the magnetic
10 depolarizer might be between 1 and 10 cm and its height in a direction above the skull could be between 0.5 to 5 cm. The length of magnetic depolarizer would typically be between 3 and 15 cm. The magnetic depolarizer could be placed within some form of head covering such as a bicycle helmet. A rechargeable battery and electronic circuitry to generate the required alternating magnetic field could also be contained within a helmet type of head gear.
15 A conventional AC adapter (recharging device) could be provided to the patient for recharging the battery of the magnetic depolarizer system.

A sufficiently intense alternating magnetic field must be created that would cause the excited band of brain neurons to be depolarized before this band has a chance to create a migraine headache. The intensity of the magnetic field at the surface of the brain should be
20 between 0.1 and 10 Tesla. The frequency rate of the magnetic pulses should be between 0.1Hz and 1.0 kHz. With some patients a single, short duration pulse may be all that is required to stop an advancing band of excited neurons from proceeding to a full-blown migraine headache. The magnetic pulses can be applied continuously for a period of between 0.1 and 100 seconds. By applying a time varying magnetic field to the neurons of the
25 cerebral cortex (and also to the neurons in the scalp), a patient could be able to actually prevent the occurrence of a migraine headache.

Thus, an objective of this invention is to prevent the occurrence of a migraine headache by creating a high intensity, time varying magnetic field by means of a magnetic depolarizer placed onto the scalp of a patient who has an aura which is a precursor of a
30 migraine headache, the magnetic depolarizer being adapted to cause depolarization of the neurons in the cerebral cortex where the aura originates.

Another object of this invention is to have the magnetic depolarizer placed inside a headgear that the patient can place on his or her head, the headgear being adapted to place the magnetic depolarizer at a specific location relative to the patient's cerebral cortex.

Still another object of the invention is to have a magnetic depolarizer system that
5 includes a battery, electronic circuitry (including a magnetic depolarizer) for creating a high intensity, time varying magnetic field, a patient operated ON-OFF switch and settings of the system's operating parameters that are set by a physician.

Still another object of the invention is to have the magnetic depolarizer system use a rechargeable battery.

10 These and other objects and advantages of this invention will become obvious to a person of ordinary skill in this art upon reading the detailed description of this invention including the associated drawings as presented herein.

BRIEF DESCRIPTION OF THE DRAWINGS

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FIGS. 1-3 are an illustration of how a band of excitable neurons spreads across the occipital lobe of a human brain.

FIG. 4 is a cross section of the present invention showing a magnetic depolarizer system within a helmet on the head of a migraine patient.

20 FIG. 5 is a longitudinal cross section of the magnetic depolarizer.

FIG. 6 is a top view of the magnetic depolarizer.

FIG. 7 is a simplified circuit diagram of the main components of a magnetic depolarizer system.

25 DETAILED DESCRIPTION OF THE INVENTION

FIGS. 1-3 illustrate a time sequence of events associated with a visual aura of a migraine headache. Initially, the brain 1 experiences a band 3 of brain neurons in an excited state. The region 2 of the brain 1 has neurons in a normal state of excitation while the region
30 4 has neurons that are in depressed state of excitation. As the aura of the migraine headache continues in time, the band 3 shown in FIG. 1 advances at a rate between 2-5 mm per minute in a direction shown by the arrow 5. In FIG. 2, we see that the band 3 has advanced in an anterior direction, and the region 4 of depressed neurons has become enlarged. Finally, in

FIG. 3, we see that the depressed region 4 has spread to occupy a majority of the neurons of the visual cortex (i.e., the occipital lobe). This phenomenon is known as "spreading depression". With a typical patient, the duration during which spreading depression occurs is between 20 and 30 minutes.

5 FIG. 4 illustrates the head of a migraine patient showing a cross section of the magnetic depolarizer system 10 as it would be contained within a helmet 11 of the type used by bicycle riders. The magnetic depolarizer system 10 consists of a magnetic depolarizer 12, a battery 14, electronic circuitry 15, a recharging receptacle 16 and interconnecting wires 17. The magnetic depolarizer system 10 is contained within the helmet 11 by means of an elastic
10 support 13 that passes between a front support 11A and a rear support 11B. The purpose of the elastic support 13 is to keep the magnetic depolarizer coil 12 in comparatively tight contact with the top and back of the patient's head and at a specific location relative to the patient's cerebral cortex.

FIG. 5 is a longitudinal cross section of the magnetic depolarizer 12 of FIG. 4. The
15 magnetic depolarizer 12 consists of a first coil 21 placed into a figure-eight configuration with a second coil 22. The two coils 21 and 22 are electrically connected in series in such a way as to create north magnetic poles 21A and 22A in essentially opposite directions when electric current is flowing through the coils 21 and 22. This orientation of coils 21 and 22 can produce a comparatively strong magnetic field onto the cortex of the brain for a distance
20 of a few centimeters beneath the cranium. If the magnetic field changes rapidly in time, it produces an electric current in the visual cortex that can cause the advancing band 3 (of FIGS. 1-2) of excited neurons (or neurons in front of the advancing band) to be depolarized thus preventing the spreading depression phenomenon from continuing. If the spreading depression can be halted, it is likely that at least some migraine patients will not develop a
25 migraine headache or possibly the headache will be less severe.

Because the helmet 11 containing the magnetic depolarizer system 10 can be kept in reasonably close proximity to the patient at all times, it would be reasonable to assume that the patient can place the helmet 11 appropriately in less than the 20 to 30 minutes that is the time period during which the pre-migraine aura occurs. It should also be understood that the
30 patient could use one or more elastic bands (without a helmet) to place the magnetic depolarizer at an appropriate location onto his or her head.

FIG. 6 is a top view of the magnetic depolarizer 12 showing as dotted lines the outline of the coils 21 and 22. In both FIGS. 5 and 6, it is shown that the coils 21 and 22 could be

encapsulated into a plastic housing 25. Furthermore, FIG. 5 shows a magnetic core 23 in the coil 21 and a separate magnetic core 24 in the coil 22. These cores 23 and 24 are not required for the device to perform its intended purpose of generating a depolarizing electric current within the cerebral cortex, but they could be used to provide the same magnetic field intensity in the brain at a lower level of electric current in the coils 21 and 22. To be effective at the high frequency of the magnetic pulses that are used to stimulate the cortex, the cores 23 and 24 would typically be formed from powdered iron or equivalent ferromagnetic material that has low eddy current and hysteresis losses.

Although FIGS. 5 and 6 show a race-track, figure eight type of design for the magnetic depolarizer 12, it should be understood that a simple cylindrical coil (and other shaped coils as well) with or without a ferromagnetic core could be used generate the desired time-varying magnetic field.

FIG. 7 is a simplified electrical diagram of the magnetic depolarizer system 10. The rechargeable battery 14 can be recharged through the receptacle 16 that can receive a plug from a conventional AC adapter (not shown) that connects to AC line voltage (e.g., 115 volts) and delivers an appropriate DC voltage to recharge the rechargeable battery 14. An adapter for utilizing a car or boat 12-volt battery for operating the magnetic depolarizer system 12 is also envisioned. When the patient is experiencing an aura of a migraine headache, he or she can throw the ON-OFF switch 29 to the ON position. That would cause the DC-to-DC converter 30 to come on and generate a high voltage for rapidly charging the capacitor 26. When the control circuitry 28 senses that the appropriate voltage has been reached, it moves the switch 27 from position A to position B thus discharging the capacitor 26 through the coils 21 and 22 of the magnetic depolarizer 12. As previously described, the coils 21 and 22 could have air cores or they could use magnetically permeable cores 23 and 24. The control circuitry 28 can be used to set the repetition rate for causing magnetic pulses to be delivered. For example, a pulse from the capacitor might last for 70 microseconds and could be repeated at a frequency rate between 0.1 and 100 Hz. A frequency of 1.0 Hz has been shown to be effective in depolarizing brain neurons and may be ideal for some migraine patients. However, other patients might find other repetition rates to be more effective. It is even possible that a single magnetic pulse having a time duration between 10 and 1,000 microseconds could be used to stop an aura thereby preventing the occurrence of a migraine headache.

Although FIGS. 4 and 7 show a battery operated magnetic depolarizer system 10, the system 10 could be operated by plugging into a receptacle at (typically) 115 or 230 volts AC. Such a system might or might not use a battery as part of its circuitry.

It should be understood that in order to be useful to a migraine patient, the magnetic depolarizer system 10 must have several distinct characteristics that are different from currently available systems for repetitive Transcranial Magnetic Stimulation (rTMS). Specifically, the inventive concept of the present invention includes the fact that the magnetic depolarizer system 10 is readily portable, has preset operating parameters that are not adjustable by the patient, can be placed on the patient's head by the patient and is turned on and off by the patient. "Readily portable" can be defined as having a weight of less than 15 kg. The only presently known rTMS equipment (the Cadwell MES-10) is operated by a physician and not by a patient, has operational parameters that are adjustable by the physician as it is being used (i.e., the parameters are not preset), has a magnetic coil that is placed on a patient by an attending physician, and since the entire system weighs 34 kg it is certainly not readily portable so as to be with the patient wherever he or she might need it. To be useful for its intended purpose, the magnetic depolarizer system 10 would have operating parameters that are preset by an attending physician. These operating parameters can include one or more of the following attributes: the peak intensity of the magnetic field at a distance of 1.0 cm beneath the magnetic depolarizer; the time period of each magnetic pulse; the repetition rate of the magnetic pulses; the total number of pulses to be delivered when the magnetic depolarizer system is turned on; and the location of the magnetic depolarizer within a helmet into which the magnetic depolarizer is placed. Once these parameters are set, the patient would operate the system 10 by placing it on his or her head and then turning the system on and then off after the aura of a migraine headache has been terminated. It may be desirable for the patient to turn the system on but a timer would automatically turn the system off after a preset period of time.

Since the aura of a migraine headache might occur at any time, and since the patient may have only 20 minutes to use the magnetic depolarizer system 10, each patient would want to have a system in relatively close proximity. For example, the patient would want to have the system at home, and/or at work, and/or in his or her car. The magnetic depolarizer system would optimally be sufficiently portable to be taken with the patient on a vacation or on a business trip.

It is also envisioned that the magnetic depolarizer system could include a memory for recording various parameters of the magnetic depolarizer system including the setting of the magnetic field intensity. Within a limited range, it is envisioned that the patient could set different levels for the magnetic field intensity in order to determine that level that is most effective in preventing a migraine headache. It is further envisioned that the magnetic depolarizer system as described herein could be used for the treatment of other disorders such as depression, pain, epilepsy, bipolar disease and other disorders of the brain.

Various other modifications, adaptations and alternative designs are of course possible in light of the teachings as presented herein. Therefore, it should be understood that, while still remaining within the scope and meaning of the appended claims, this invention could be practiced in a manner other than that which is specifically described herein.

What is claimed is:

1. A magnetic depolarizer system for the treatment of migraine headache, the system comprising:

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a readily portable magnetic depolarizer adapted for placement at a specific location onto the head of a human being, the magnetic depolarizer having a least one electromagnetic coil that is capable of providing a time varying magnetic field having a peak intensity at some portion of the patient's cerebral cortex of at least 0.1 Tesla;

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electrical circuitry connected to the magnetic depolarizer for providing an electrical current through the at least one electromagnetic coil, the electrical circuitry also including a patient operated switch for turning on the magnetic depolarizer system; and,

15

a positioner adapted to affix the magnetic depolarizer system onto a specific region of the head of the human being.

2. The system of claim 1 wherein the electrical circuitry of the magnetic depolarizer system includes a battery.

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3. The system of claim 2 wherein the battery is rechargeable.

4. The system of claim 1 wherein the magnetic depolarizer includes at least two coils, in a race-track, figure-eight configuration.

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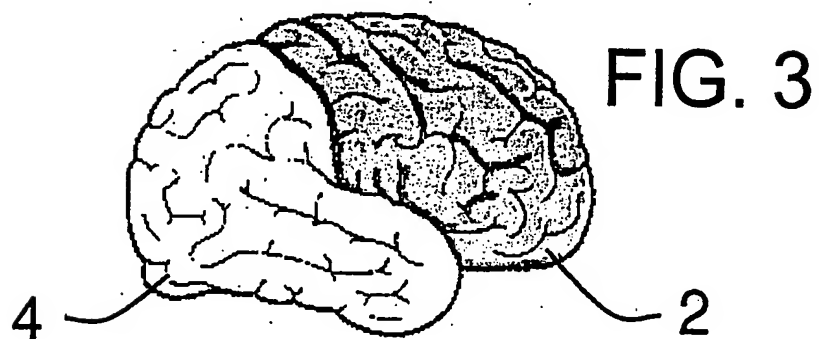
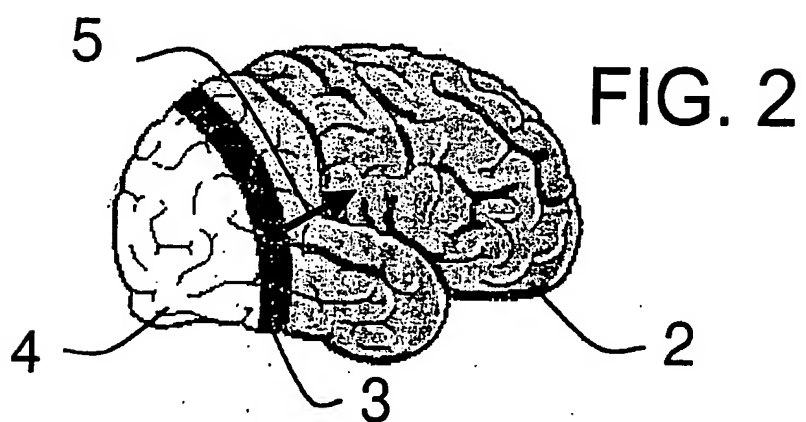
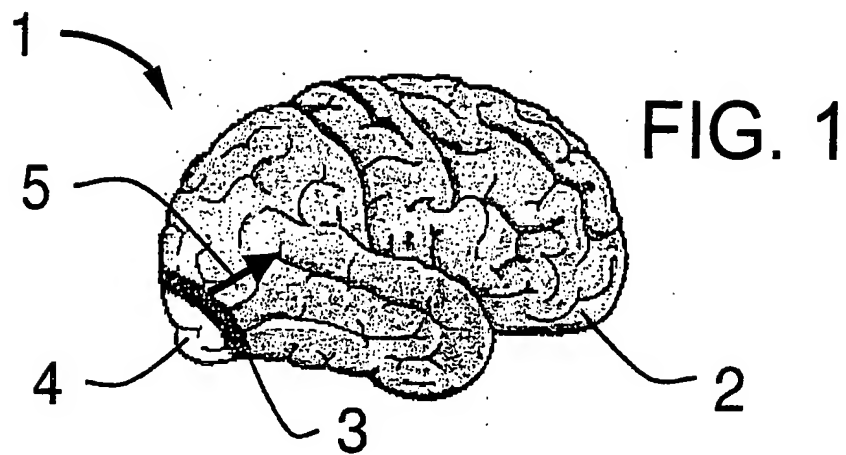
5. The system of claim 1 wherein the magnetic depolarizer includes at least one ferromagnetic core.

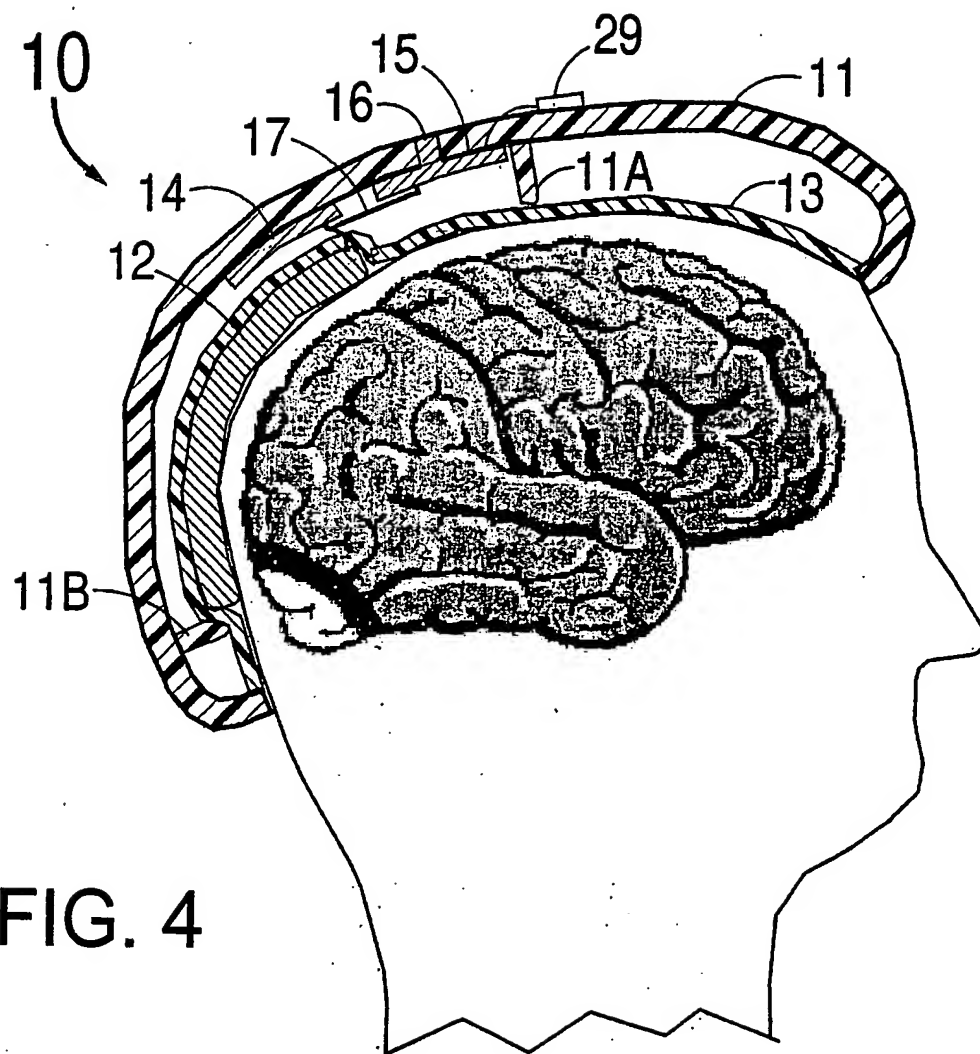
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6. The system of claim 1 wherein the electronic circuitry is adapted to deliver at least one time varying magnetic pulse.

7. The system of claim 6 wherein the length of the magnetic pulse is between approximately 1 microsecond and approximately 1,000 microseconds.

8. The system of claim 6 wherein the electronic circuitry is adapted to deliver a sequence of pulses comprising a plurality of time varying magnetic pulses, and wherein the magnetic pulses are delivered at a rate of between approximately 0.1 Hz and approximately 1,000 Hz.
9. The system of claim 8 wherein the sequence of pulses is delivered over a time period of between approximately 0.1 second and approximately 100 seconds.
10. The system of claim 1 wherein the positioner comprises a headgear adapted to accurately place the magnetic depolarizer at a specific location on the head of the human being.
11. The system of claim 10 wherein the headgear comprises a helmet of the type worn by bicycle riders.
12. The system of claim 10 wherein the headgear comprises at least one elastic band.
13. The system of claim 1, wherein the electrical circuitry also includes at least one operating parameter that is preset by a physician
14. A system for the treatment of a migraine headache in a patient, the system comprising:
- a readily portable magnetic depolarizer adapted for placement at a specific location onto the head of the patient, wherein the magnetic depolarizer is capable of providing a time varying magnetic field having a peak intensity at some portion of the patient's cerebral cortex of at least 0.1 Tesla;
- a patient-operated switch for activating the magnetic depolarizer; and
- a positioner for placing the magnetic depolarizer onto a specific region of the head of the patient.





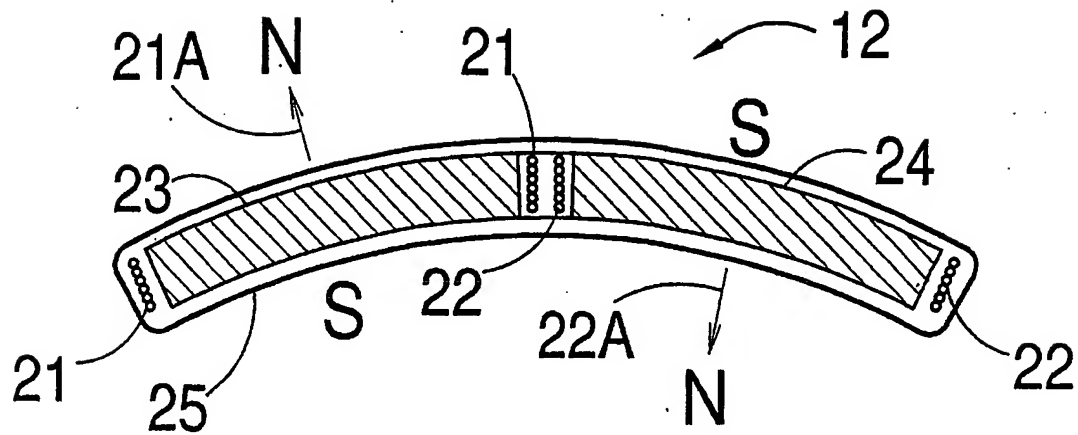


FIG. 5

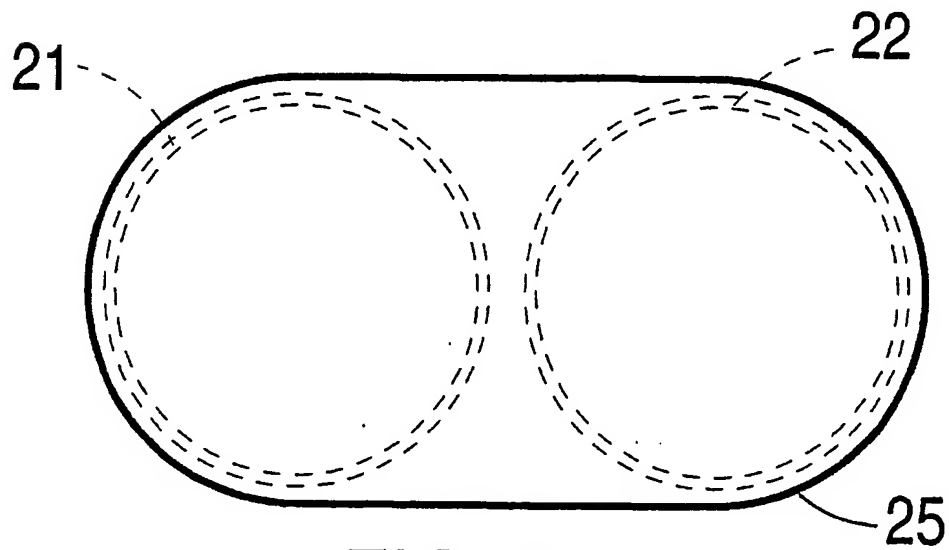


FIG. 6

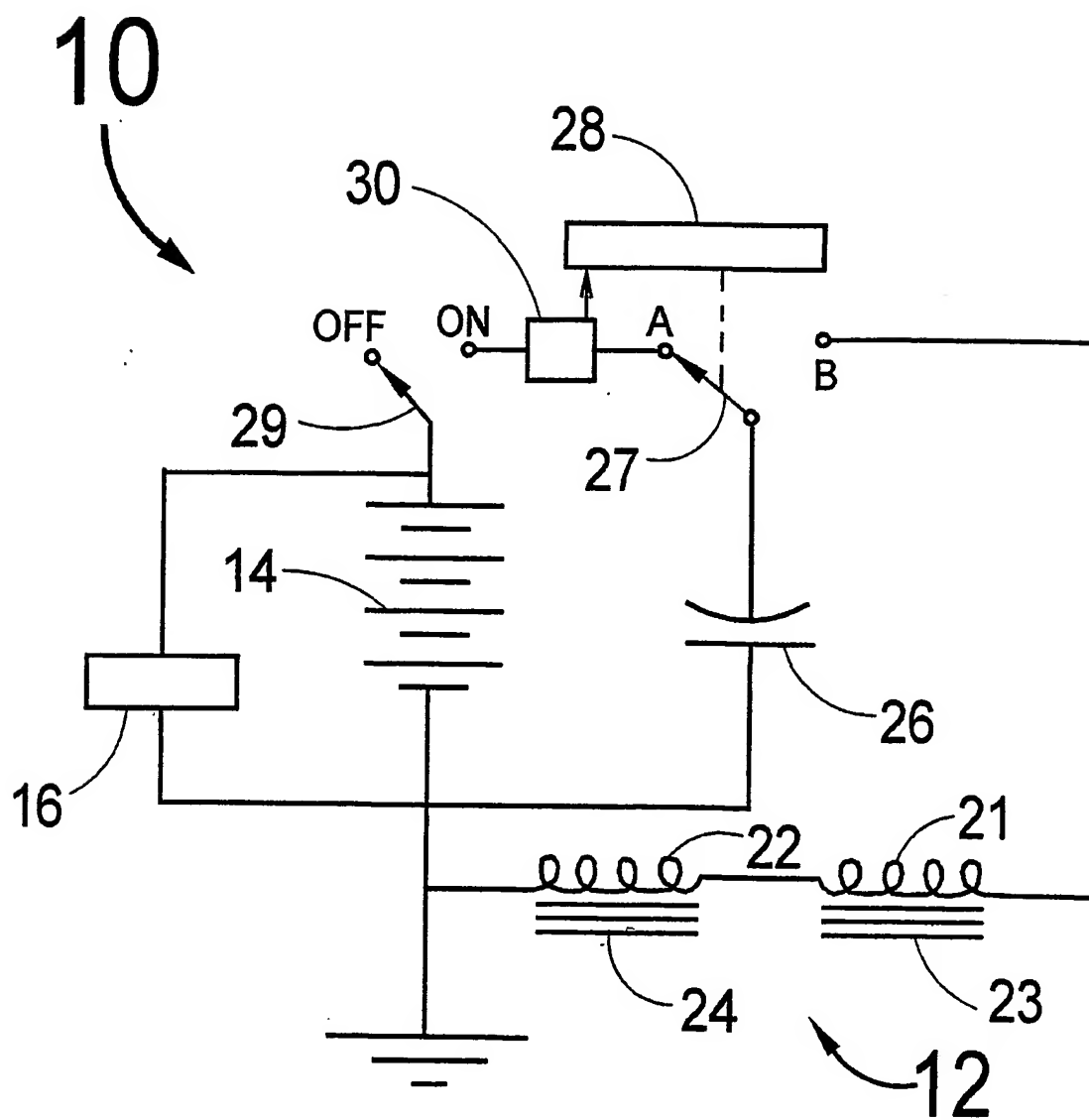


FIG. 7

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 01/23958

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61N2/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 98 06342 A (EPSTEIN CHARLES M ; DAVEY KENT R (US); NEOTONUS INC (US)) 19 February 1998 (1998-02-19) page 6, line 17 -page 8, line 28; figures	1,14
A	DE 198 15 900 A (WOLFF FRIEDRICH) 1 July 1999 (1999-07-01) column 1, line 51 -column 7, line 42; figures	1,14
A	GB 2 271 931 A (SACKS BENJAMIN ISRAEL ; RUDOLF NOEL (GB)) 4 May 1994 (1994-05-04) page 3, line 1 -page 5, line 9; figures	1,14
A	US 5 738 625 A (GLUCK DANIEL S) 14 April 1998 (1998-04-14) column 3, line 16 -column 4, line 30; figures	1,14

☐ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

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Date of the actual completion of the international search

26 November 2001

Date of mailing of the international search report

30/11/2001

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INTERNATIONAL SEARCH REPORT

Information on patent family members

Int. Patent Application No

PCT/US 01/23958

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9806342	A	19-02-1998	AU 735591 B2	12-07-2001
			AU 4158497 A	06-03-1998
			EP 0930849 A1	28-07-1999
			JP 2000504966 T	25-04-2000
			WO 9806342 A1	19-02-1998
			US 6132361 A	17-10-2000
DE 19815900	A	01-07-1999	DE 19815900 A1	01-07-1999
			WO 9932191 A1	01-07-1999
GB 2271931	A	04-05-1994	NONE	
US 5738625	A	14-04-1998	DE 4420233 A1	15-12-1994
			GB 2278783 A	14-12-1994
			JP 7143971 A	06-06-1995

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